UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,772	05/26/2005	Jianren Gu	186691/US	4584

25763 7590 04/17/2007

DORSEY & WHITNEY LLP
INTELLECTUAL PROPERTY DEPARTMENT
SUITE 1500
50 SOUTH SIXTH STREET
MINNEAPOLIS, MN 55402-1498

EXAMINER	
REDDIG, PETER J	
ART UNIT	**PAPER NUMBER**
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,772	GU ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *3-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 May 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/26/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

1. The response filed on 3/28/2007 to the restriction requirement of February 27, 2007 has been received. Applicant has elected Group 1, claims 1 and 2 for examination without traverse.

2. Claims 1-10 are pending.

3. It is noted that in the remarks of March 28, 2007 Applicant state that claims 3-10 have been cancelled, but the claim set of March 28, 2007 identifies claims 3-10 as withdrawn. Clarification is required. It will be assumed for examination purposes that claims 3-10 are withdrawn. Claims 3-10 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

4. Claims 1 and 2 are currently under consideration.

Specification

5. The specification is objected for improper disclosure of amino acid sequences without a respective sequence identifier, i.e. a SEQ ID NOs: in Figure 1. Hence, the disclosure fails to comply with the requirements of 37 CFR 1.821 through 1.825. In the absence of a sequence identifier for each sequence, Applicant must provide a computer readable form (CRF) copy of the sequence listing, an initial or substitute paper copy of the sequence listing, as well as any amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e-f) or 1.825(b) or 1.825(d). *Failure to supply the appropriate sequences identification numbers in response to this action will be considered non-responsive.*

Priority

5. It is noted that examiner has established a priority date for the instant application,

10/536,772, of May 26, 2005 because the priority of the instantly claimed invention is based on the Chinese patent, number PCT/CN03/00845, which has not been translated and examiner is unable to determine the information in the document. If applicant disagrees with any rejection set forth in this action based on examiner's establishment of a priority date, of May 26, 2005, for the instantly claimed application serial number 10/526,741, applicant is invited to submit a proper translation of the priority document and to point to, page and line where support can be found establishing an earlier priority date.

Drawings

6. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: "forward", "reverse", and "empty" in Figure 4 and "empty" in Figure 5. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

7. The drawings are objected to because the y-axis of the graph in figure 4 is not labeled. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office

action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

8. Claim 2 is objected to because of the following informalities: The word "cell" should be "cells". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated human CT120 protein polypeptide comprising or having the amino acid sequence of SEQ ID NO: 2 *does not* reasonably provide enablement for

an isolated human CT120 protein polypeptide comprising a conservative variant polypeptide, active fragment or active derivative of SEQ ID NO: 2 or SEQ ID NO: 2 with one or more substitution, deletion or insertion in the amino acid residues which has the function of promoting the growth of NIH/3T3 cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986).

The claims are drawn to an isolated human CT120 protein polypeptide comprising the amino acid sequence of SEQ ID NO: 2, or its conservative variant polypeptide, active fragment or active derivative and the polypeptide of claim 1, wherein said polypeptide is selected from the following group: (a) a polypeptide having the amino acid sequence of SEQ ID NO: 2; (b) a polypeptide derived from the polypeptide (a) with one or more substitution, deletion or insertion in the amino acid residues of polypeptide (a), which has the function of promoting the growth of NIH/3T3 cell.

This means that *any* conservative variant polypeptide, active fragment or active derivative of SEQ ID NO: 2 or *any* SEQ ID NO: 2 with one or more substitution, deletion or insertion in the amino acid residues of polypeptide will function as contemplated in the specification and claimed as a promoter of NIH/3T3 cell growth.

The specification teaches that CT120/SEQ IDNO: 2 gene was cloned by the identification of cDNAs and expressed sequence tags that correspond to the region of chromosome 17 (17p13.3) that is frequently lost in hepatocellular carcinoma, see p. 3, lines 28-36 and Examples 1 and 2. The specification teaches that expression of CT120/SEQ ID NO: 2 by transient transfection in NIH3T3 cells promoted the growth/transformation, see p. 3, lines 39-40, see p. 18, lines 38-39, and Figure 4. The specification teaches that CT120/SEQ ID NO: 2 is expressed in pulmonary cancer and not in tissue near the pulmonary cancer, see p.19, lines 21-23 and Figure 6.

The specification teaches that a "conservative mutant of human tumor related protein CT120" means a polypeptide formed by substituting at most 10, preferably at most 8, more preferably 5, and most preferably at most 3 amino acids with the amino acids having substantially the same or similar property, as compared with the amino acid sequence of SEQ ID NO: 2. Preferably, these conservative mutants are formed by the substitution according to Table 1, see para. bridging p.4 and 5. However, the specification does not define "conservative variant polypeptides and, thus a conservative variant polypeptide of SEQ ID NO: 2 will be interpreted for examination purposes to encompass any conservative variant of SEQ ID NO: 2.

One cannot extrapolate the teachings to the scope of the claims because the claims are inclusive of multiple variants of SEQ ID NO: 2 and the specification has not established a nexus

between these variant forms of SEQ ID NO: 2, and as drawn to claim 1, has not established that there is a differential expression of the variants polypeptides in cancer compared to normal control as contemplated in the specification or established that the claimed variants promote the growth of NIH/3T3 cells and as drawn to claim 2, has not established that the claimed variants promote the growth of NIH/3T3 cells. Furthermore, one of skill in the art could not predictably establish a nexus between all of the variants of SEQ ID NO: 2 contemplated in the specification and claimed and promoting the growth of NIH/3T3 cells or differential expression in cancer because 1) the claims encompass undefined variants with unknown identity to SEQ ID NO: 2 and the sequences critical for the contemplated and claimed functions are unknown and the unpredictability of predicting function from structure in protein biochemistry is well known in the art 2) the heterogeneity of cancer is well known in the art and any nexus between the differential expression of SEQ ID NO: 2 and pulmonary cancer would not be predictably extrapolated to the various forms of SEQ ID NO: 2 contemplated and claimed and one could not predictably use the variants of SEQ ID NO: 2 to distinguish cancer tissue from normal tissue .

1) As drawn to the unpredictability of protein biochemistry, Bowie et al (Science, 1990, 257:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (col. 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's

sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col. 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. Further, Scott et al (Nature Genetics, 1999, 21:440-443) teach that the gene causing Pendred syndrome encodes a putative transmembrane protein designated pendrin. Based on sequence similarity data, the authors postulated that the putative protein was deemed to be a member of sulfate transport protein family since the putative protein had a 29% identity to rat sulfate-anion transporter, 32% similarity to human diastrophic dysplasia sulfate transporter and 45% similarity to the human sulfate transporter. However, upon analyzing the expression and kinetics of the protein, the data revealed no evidence of sulfate transport activity wherein results revealed that pendrin functioned as a transporter of chloride and iodide. Scott et al suggest that these results underscore the importance of confirming the function of newly identified gene products even when database searched reveal significant homology to proteins of known function (page 411, 1st column, 4th paragraph). In addition, Bork (Genome Research, 2000,10:398-400) clearly

teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, col 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, col 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, col 3). Further, although gene annotation via sequence database searches is already a routine job, even here the error rate is considerable (p. 399, col 2). Most features predicted with an accuracy of greater than 70% are of structural nature and at best only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399 para bridging cols 2 and 3). The reference finally cautions that although the current methods seem to capture important features and explain general trends, 30% of those features are missing or predicted wrongly. This has to be kept in mind when processing the results further (p. 400, para bridging cols 1 and 2). The teachings of Bork are clearly illustrated by Pero et al. (US PG Pub 20030105000) who specifically teach in Example 4 that the SH2 domain of Grb14 is 81% similar to the SH2 domain of Grb7 on the amino acid level, but although Grb7 binds to ErbB2, Grb14 does not bind to ErbB2. Further, although the SH2 domain of Grb2 is only 50 % similarity to Grb 7 on the amino acid level, both Grb2 and Grb7

bind to the same site on ErbB2. Thus, sequence identity or similarity alone cannot be used to predict the function of a protein.

Although conservative substitutions increase the chance of having less effect on the activity of the protein, it is unpredictable which amino acid at a certain position could be subtituted even by conservative substitution. For example, Straub P et al, 1993, J Biol Chem 268(29): 21997-20003, teach that conservative substitutions of valine for glycine at positions 111 and 117 of cytochrome P450 2C2 result in about 50- and 7-fold reduction of activity, respectively. Kouklis PD et al, 1993, J Cell Science, 106(pt 3): 919-28, teach that a single exchange of glycine 450 of the intermediate filament protein vimentin with valine strongly interfers with the normal assembly of the intermediate filaments.

Given that the claims encompass undefined variants with unknown identity to SEQ ID NO: 2, and given that no information has been set forth drawn to the amino acids critical to the function of SEQ ID NO: 2, one would not know how to make the claimed invention so that it would predictably function as contemplated or claimed or how to identify those variants that will function as contemplated or claimed. Thus undue experimentation would be required to make and use the variants of SEQ ID NO: 2 encompassed by the claims.

2) As drawn to cancer heterogeneity, cancers comprise a broad group of malignant neoplasms divided into two categories, carcinoma and sarcoma. The carcinomas originate in epithelial tissues while sarcomas develop from connective tissues, see Taber's Cyclopedic Medical Dictionary (1985, F.A. Davis Company, Philadelphia, p. 274). Given that not all cancers originate from the same tissue types, it is expected and known that cancers originate from different tissue types have different structures as well as etiologies and would present differently.

Thus, it would not be predictably expected that a nexus, for example drawn to a connection between SEQ ID NO: 2 and pulmonary cancer, would be established between two cancer types that arose from different tissue types for the variants of SEQ ID NO: 2 contemplated and claimed. Further, it is well known that even two carcinomas that present on the same organ have significant differences in etiology and genetic constitution. For example, Busken, C et al, (Digestive Disease Week Abstracts and Itinerary Planner, 2003, abstract No:850), teach that there is a difference in COX-2 expression with respect to intensity, homogeneity, localization and prognostic significance between adenocarcinoma of the cardia and distal esophagus, suggesting that these two cancers have different etiology and genetic constitution (last five lines of the abstract). Furthermore Krontiris and Capizzi (Internal Medicine, 4th Edition, Editor-in-chief Jay Stein, Elsevier Science, 1994 Chapters 71-72, pages 699-729) teach that the various types of cancers have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocols. Given the above, it is clear that it is not possible to predictably extrapolate a correlation between SEQ ID NO: 2 and differential expression in pulmonary cancer and all of the variants of SEQ ID NO: 2 contemplated and claimed in any tumor type, based on the information in the specification and known in the art without undue experimentation.

Given the above teachings, the ability of the variants of CT120/SEQ ID NO: 2 encompassed by the claims and contemplated in the specification to promote the growth of NIH/3T3 cells or be differentially expressed in cancers could not be predicted, based on sequence similarity to SEQ ID NO: 2. Given the above, it is clear that undue experimentation would be required of one of skill in the art to make and use the full scope of encompassed by the

claims CT120/SEQ ID NO: 2 proteins that promote the growth of NIH/3T3cells or are differentially expressed in cancers. Thus, it would take undue experimentation for one of ordinary skill in the art to make and use the invention as claimed.

Applicant is reminded that MPEP 2164.03 teaches "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 428 F.2d 833, 166 USPQ 18, 24 (CCPA 1970) the amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly state in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order for it to be enabling. Given only lack of guidance in the specification, no one skilled in the art would accept the assertion that the claimed invention would function as contemplated or as claimed based only on the information in the specification and that known in the art at the time the invention was made.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention will function as contemplated or claimed with a reasonable expectation of success. For the above reasons, it appear that undue experimentation would be required to practice the claimed invention.

10. Claims 1 and 2 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

The state of the art is such that it is well know in the art that protein biochemistry is unpredictable and, thus, predicting protein function from structure is unpredictable.
In particular, Bowie et al (Science, 1990, 257:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (col. 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col. 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological

activity of the mitogen. Thus, given the above, it is clear that in the protein biochemistry arts an adequate written description is essential for one of skill in the art to make and use the claimed invention.

Claims 1 and 2 are broadly drawn to an isolated human CT120 protein polypeptide comprising the amino acid sequence of SEQ ID NO: 2, or its conservative variant polypeptide, active fragment or active derivative and the polypeptide of claim 1, wherein said polypeptide is selected from the following group: (a) a polypeptide having the amino acid sequence of SEQ ID NO: 2; (b) a polypeptide derived from the polypeptide (a) with one or more substitution, deletion or insertion in the amino acid residues of polypeptide (a), which has the function of promoting the growth of NIH/3T3 cell.

It is noted that the specification does not define "conservative variant polypeptides and, thus a conservative variant polypeptide of SEQ ID NO: 2 will be interpreted for examination purposes to encompass any conservative variant of SEQ ID NO: 2.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

Thus, the instant specification may provide an adequate written description of a CT120 polypeptide comprising a conservative variant polypeptide, active fragment or active derivative of the amino acid sequence of SEQ ID NO: 2 or a polypeptide derived from the SEQ ID NO: 2 with one or more substitution, deletion or insertion in the amino acid residues of SEQ ID NO: 2 which has the function of promoting the growth of NIH/3T3 cells, per Lilly by structurally describing a representative number of CT120 polypeptides comprising a conservative variant polypeptide, active fragment or active derivative of the amino acid sequence of SEQ ID NO: 2 or polypeptides derived from the SEQ ID NO: 2 with one or more substitution, deletion or insertion in the amino acid residues of SEQ ID NO: 2 which has the function of promoting the growth of NIH/3T3 cells, or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe a CT120 polypeptide comprising a conservative variant polypeptide, active fragment or active derivative of the amino acid sequence of SEQ ID NO: 2 or a polypeptide derived from the SEQ ID NO: 2 with one or more substitution, deletion or insertion in the amino acid residues of SEQ ID NO: 2 which has the function of promoting the growth of NIH/3T3 cells, in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any CT120

polypeptide comprising a conservative variant polypeptide, active fragment or active derivative of the amino acid sequence of SEQ ID NO: 2 or a polypeptide derived from the SEQ ID NO: 2 with one or more substitution, deletion or insertion in the amino acid residues of SEQ ID NO: 2 which has the function of promoting the growth of NIH/3T3 cells, nor does the specification provide any partial structure of such polypeptides, nor any physical or chemical characteristics of a CT120 polypeptide comprising a conservative variant polypeptide, active fragment or active derivative of the amino acid sequence of SEQ ID NO: 2 or a polypeptide derived from the SEQ ID NO: 2 with one or more substitution, deletion or insertion in the amino acid residues of SEQ ID NO: 2 which has the function of promoting the growth of NIH/3T3 cells, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. It is noted that claim 1, although drawn to conservative variant polypeptides, active fragments or active derivatives, does not recite any function associated with the claimed invention. Although the specification discloses SEQ ID NO: 2, this does not provide a description of a CT120 polypeptide comprising a conservative variant polypeptide, active fragment or active derivative of the amino acid sequence of SEQ ID NO: 2 to which no function has been ascribed or a polypeptide derived from the SEQ ID NO: 2 with one or more substitution, deletion or insertion in the amino acid residues of SEQ ID NO: 2 which has the function of promoting the growth of NIH/3T3 cells that would satisfy the standard set out in Enzo.

The specification also fails to describe a CT120 polypeptide comprising a conservative variant polypeptide, active fragment or active derivative of the amino acid sequence of SEQ ID NO: 2 or a polypeptide derived from the SEQ ID NO: 2 with one or more substitution, deletion or insertion in the amino acid residues of SEQ ID NO: 2 which has the function of promoting the

growth of NIH/3T3 cells by the test set out in Lilly. The specification describes only SEQ ID NO: 2. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of a CT120 polypeptide comprising a conservative variant polypeptide, active fragment or active derivative of the amino acid sequence of SEQ ID NO: 2 or a polypeptide derived from the SEQ ID NO: 2 with one or more substitution, deletion or insertion in the amino acid residues of SEQ ID NO: 2 which has the function of promoting the growth of NIH/3T3 cells that is required to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by He et al. (Biochem. Biophys. Res. Com., September 27, 2002, 297:528-536, IDS) as evidenced by the alignment 1, FA57A_HUMAN in the Appendix.

The claims are drawn to 1. An isolated human CT120 protein polypeptide comprising the amino acid sequence of SEQ ID NO: 2, or its conservative variant polypeptide, active fragment or active derivative. 2. The polypeptide of claim 1, wherein said polypeptide is selected from the following group: (a) a polypeptide having the amino acid sequence of SEQ ID NO: 2; (b) a

polypeptide derived from the polypeptide (a) with one or more substitution, deletion or insertion in the amino acid residues of polypeptide (a), which has the function of promoting the growth of NIH/3T3 cell.

He et al. teach a CT120 protein that is 99.1% identical to SEQ ID NO: 2, see Figure 1 and alignment 1.

As drawn to claim 1, the product of the prior art comprises the same product as claimed in the instant invention, that is an isolated human CT120 protein polypeptide comprising the amino acid sequence of SEQ ID NO: 2, or its conservative variant polypeptide, active fragment or active derivative. As drawn to claim 2, the product of the prior art is clearly derived from SEQ ID NO: 2 with one or more substitutions. Given that there is 99.1% identity between SEQ ID NO: 2 and the product of the prior art, it would be expected that the claimed product has the same function and will promote the growth of NIH-3T3 cells. Although the reference does not specifically state that the CT120 protein promotes NIH-3T3 cell growth, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

12. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by He et al. (Chinese Journal of Cancer, February, 2003, 22:113-8).

The claims are drawn to 1. An isolated human CT120 protein polypeptide comprising the amino acid sequence of SEQ ID NO: 2, or its conservative variant polypeptide, active fragment or active derivative. 2. The polypeptide of claim 1, wherein said polypeptide is selected from the following group: (a) a polypeptide having the amino acid sequence of SEQ ID NO: 2; (b) a polypeptide derived from the polypeptide (a) with one or more substitution, deletion or insertion in the amino acid residues of polypeptide (a), which has the function of promoting the growth of NIH/3T3 cell.

He et al. teach a CT120 membrane-associated protein that was cloned from the chromosome 17p13.3 locus. He et al. teach that CT120 promoted the proliferation of NIH3T3 cells in vitro in the colony forming assay, see Abstract.

Although He et al. do not teach the sequence of CT120, the CT120 gene was isolated from the same source, the locus 17p13.3, as SEQ ID NO: 2 and it performs the same function as SEQ ID NO: 2, promoting growth of NIH/3T3 cells, thus the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

13 Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Ruben et al. (WO/2000/035937, June 22, 2000) as evidenced by the alignment 2, AAB24463 in the Appendix.

The claims are drawn to 1. An isolated human CT120 protein polypeptide comprising the amino acid sequence of SEQ ID NO: 2, or its conservative variant polypeptide, active fragment or active derivative. 2. The polypeptide of claim 1, wherein said polypeptide is selected from the following group: (a) a polypeptide having the amino acid sequence of SEQ ID NO: 2; (b) a polypeptide derived from the polypeptide (a) with one or more substitution, deletion or insertion in the amino acid residues of polypeptide (a), which has the function of promoting the growth of NIH/3T3 cell.

Ruben et al. teach a protein that is 99.1% identical to SEQ ID NO: 2, see SEQ ID NO: 88, and alignment 2 in the Appendix.

As drawn to claim 1, the product of the prior art comprises the same product as claimed in the instant invention, that is an isolated human CT120 protein polypeptide comprising the amino acid sequence of SEQ ID NO: 2, or its conservative variant polypeptide, active fragment or active derivative. As drawn to claim 2, the product of the prior art is clearly derived from SEQ ID NO: 2 with one or more substitutions. Given that there is 99.1% identity between SEQ ID NO: 2 and the product of the prior art, it would be expected that the claimed product has the same function and will promote the growth of NIH-3T3 cells. Although the reference does not specifically state that the CT120 protein promotes NIH-3T3 cell growth, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order

to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

14. If applicant disagrees with any rejection set forth in this office action based on examiner's establishment of a priority date 5/26/2005 for the instantly claimed application serial number 10/536,772, applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

15. No claims allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

Peter J. Reddig, Ph.D.
Examiner
Art Unit 1642

PJR

Appendix

Alignment 1
FA57A_HUMAN

```
ID   FA57A_HUMAN     STANDARD;      PRT;   257 AA.
AC   Q8TBR7; Q7Z464; Q96D97; Q9H6H3;
DT   29-AUG-2003, integrated into UniProtKB/Swiss-Prot.
DT   12-APR-2005, sequence version 2.
DT   13-JUN-2006, entry version 32.
DE   Protein FAM57A (CT120 protein).
GN   Name=FAM57A;
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
OC   Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM 2), INTERACTION WITH GGTL3 AND
RP   SLC3A2, AND TISSUE SPECIFICITY.
RX   MEDLINE=22230983; PubMed=12270127; DOI=10.1016/S0006-291X(02)02227-1;
RA   He X.H., Di Y., Li J., Xie Y., Tang Y., Zhang F., Wei L., Zhang Y.,
RA   Qin W.X., Huo K., Li Y., Wan D.F., Gu J.R.;
RT   "Molecular cloning and characterization of CT120, a novel membrane-
RT   associated gene involved in amino acid transport and glutathione
RT   metabolism.";
RL   Biochem. Biophys. Res. Commun. 297:528-536(2002).
RN   [2]
RP   NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM 2).
RX   PubMed=14702039; DOI=10.1038/ng1285;
RA   Ota T., Suzuki Y., Nishikawa T., Otsuki T., Sugiyama T., Irie R.,
RA   Wakamatsu A., Hayashi K., Sato H., Nagai K., Kimura K., Makita H.,
RA   Sekine M., Obayashi M., Nishi T., Shibahara T., Tanaka T., Ishii S.,
RA   Yamamoto J., Saito K., Kawai Y., Isono Y., Nakamura Y., Nagahari K.,
RA   Murakami K., Yasuda T., Iwayanagi T., Wagatsuma M., Shiratori A.,
RA   Sudo H., Hosoiri T., Kaku Y., Kodaira H., Kondo H., Sugawara M.,
```

```
RA   Takahashi M., Kanda K., Yokoi T., Furuya T., Kikkawa E., Omura Y.,
RA   Abe K., Kamihara K., Katsuta N., Sato K., Tanikawa M., Yamazaki M.,
RA   Ninomiya K., Ishibashi T., Yamashita H., Murakawa K., Fujimori K.,
RA   Tanai H., Kimata M., Watanabe M., Hiraoka S., Chiba Y., Ishida S.,
RA   Ono Y., Takiguchi S., Watanabe S., Yosida M., Hotuta T., Kusano J.,
RA   Kanehori K., Takahashi-Fujii A., Hara H., Tanase T.-O., Nomura Y.,
RA   Togiya S., Komai F., Hara R., Takeuchi K., Arita M., Imose N.,
RA   Musashino K., Yuuki H., Oshima A., Sasaki N., Aotsuka S.,
RA   Yoshikawa Y., Matsunawa H., Ichihara T., Shiohata N., Sano S.,
RA   Moriya S., Momiyama H., Satoh N., Takami S., Terashima Y., Suzuki O.,
RA   Nakagawa S., Senoh A., Mizoguchi H., Goto Y., Shimizu F., Wakebe H.,
RA   Hishigaki H., Watanabe T., Sugiyama A., Takemoto M., Kawakami B.,
RA   Yamazaki M., Watanabe K., Kumagai A., Itakura S., Fukuzumi Y.,
RA   Fujimori Y., Komiyama M., Tashiro H., Tanigami A., Fujiwara T.,
RA   Ono T., Yamada K., Fujii Y., Ozaki K., Hirao M., Ohmori Y.,
RA   Kawabata A., Hikiji T., Kobatake N., Inagaki H., Ikema Y., Okamoto S.,
RA   Okitani R., Kawakami T., Noguchi S., Itoh T., Shigeta K., Senba T.,
RA   Matsumura K., Nakajima Y., Mizuno T., Morinaga M., Sasaki M.,
RA   Togashi T., Oyama M., Hata H., Watanabe M., Komatsu T.,
RA   Mizushima-Sugano J., Satoh T., Shirai Y., Takahashi Y., Nakagawa K.,
RA   Okumura K., Nagase T., Nomura N., Kikuchi H., Masuho Y., Yamashita R.,
RA   Nakai K., Yada T., Nakamura Y., Ohara O., Isogai T., Sugano S.;
RT   "Complete sequencing and characterization of 21,243 full-length human
RT   cDNAs.";
RL   Nat. Genet. 36:40-45(2004).
RN   [3]
RP   NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORMS 1 AND 2).
RC   TISSUE=Lung;
RX   MEDLINE=22388257; PubMed=12477932; DOI=10.1073/pnas.242603899;
RA   Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA   Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA   Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA   Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA   Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA   Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA   Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA   Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA   Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA   Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA   Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA   Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA   Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA   Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA   Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA   Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA   Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
RT   "Generation and initial analysis of more than 15,000 full-length human
RT   and mouse cDNA sequences.";
RL   Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
CC   -!- SUBUNIT: Interacts with GGTL3 isoform 5 and SLC3A2.
CC   -!- SUBCELLULAR LOCATION: Cell membrane; multi-pass membrane protein.
CC   -!- ALTERNATIVE PRODUCTS:
CC       Event=Alternative splicing; Named isoforms=2;
CC       Name=2; Synonyms=CT120A;
```

```
CC         IsoId=Q8TBR7-2; Sequence=Displayed;
CC       Name=1; Synonyms=CT120B;
CC         IsoId=Q8TBR7-1; Sequence=VSP_008149;
CC   -!- TISSUE SPECIFICITY: Highly expressed in pancreas. Detected at
CC       intermediate levels in heart, placenta and kidney, and at low
CC       levels in brain, liver and skeletal muscle. Not detected in normal
CC       lung.
CC   -!- SIMILARITY: Contains 1 TLC (TRAM/LAG1/CLN8) domain.
CC   ---------------------------------------------------------------------
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ---------------------------------------------------------------------
DR   EMBL; AF477201; AAM90843.1; -; mRNA.
DR   EMBL; AK025935; BAB15286.1; -; mRNA.
DR   EMBL; BC009729; AAH09729.1; -; mRNA.
DR   EMBL; BC026023; AAH26023.1; -; mRNA.
DR   UniGene; Hs.154396; -.
DR   Ensembl; ENSG00000167695; Homo sapiens.
DR   HGNC; HGNC:29646; FAM57A.
DR   RZPD-ProtExp; IOH12439; -.
DR   RZPD-ProtExp; V1526; -.
DR   RZPD-ProtExp; Z0423; -.
DR   InterPro; IPR006634; TLC.
DR   SMART; SM00724; TLC; 1.
DR   PROSITE; PS50922; TLC; 1.
KW   Alternative splicing; Membrane; Transmembrane.
FT   CHAIN         1    257       Protein FAM57A.
FT                                /FTId=PRO_0000185540.
FT   TRANSMEM      1     21       Potential.
FT   TRANSMEM     42     62       Potential.
FT   TRANSMEM     77     97       Potential.
FT   TRANSMEM    113    135       Potential.
FT   TRANSMEM    142    162       Potential.
FT   TRANSMEM    181    201       Potential.
FT   TRANSMEM    220    240       Potential.
FT   DOMAIN       33    249       TLC.
FT   VAR_SEQ     137    168       Missing (in isoform 1).
FT                                /FTId=VSP_008149.
FT   CONFLICT     25     25       R -> H (in Ref. 1).
FT   CONFLICT    129    129       F -> L (in Ref. 1).
SQ   SEQUENCE   257 AA;  29383 MW;  C799BF7143A6DA01 CRC64;

  Query Match             99.1%;  Score 1355;  DB 1;  Length 257;
  Best Local Similarity   99.2%;  Pred. No. 1.9e-116;
  Matches  255;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps
0;

Qy          1 MLLTLAGGALFFPGLFALCTWALRHSQPGWSRTDCVMISTRLVSSVHAVLATGSGIVIIR 60
              ||||||||||||||||||||||| ||||||||||||||||||||||||||||||||||||
Db          1 MLLTLAGGALFFPGLFALCTWALRRSQPGWSRTDCVMISTRLVSSVHAVLATGSGIVIIR 60

Qy         61 SCDDVITGRHWLAREYVWFLIPYMIYDSYAMYLCEWCRTRDQNRAPSLTLRNFLSRNRLM 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 SCDDVITGRHWLAREYVWFLIPYMIYDSYAMYLCEWCRTRDQNRAPSLTLRNFLSRNRLM 120
```

```
Qy        121 ITHHAVILLVLVPVAQRLRGDLGDFFVGCIFTAELSTPFVSLGRVLIQLKQQHTLLYKVN 180
              |||||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 ITHHAVILFVLVPVAQRLRGDLGDFFVGCIFTAELSTPFVSLGRVLIQLKQQHTLLYKVN 180

Qy        181 GILTLATFLSCRILLFPFMYWSYGRQQGLSLLQVPFSIPFYCNVANAFLVAPQIYWFCLL 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 GILTLATFLSCRILLFPFMYWSYGRQQGLSLLQVPFSIPFYCNVANAFLVAPQIYWFCLL 240

Qy        241 CRKAVRLFDTPQAKKDG 257
              |||||||||||||||||
Db        241 CRKAVRLFDTPQAKKDG 257
```

Alignment 2
AAB24463

```
ID   AAB24463 standard; protein; 258 AA.
XX
AC   AAB24463;
XX
DT   20-NOV-2000  (first entry)
XX
DE   Human secreted protein sequence encoded by gene 27 SEQ ID NO:88.
XX
KW   Human; secreted protein; cytostatic; antianaemic; antidiabetic;
KW   antiinflammatory; ophthalmological; antirheumatic; antiarthritic;
KW   antipsoriatic; antiangiogenic; cardiant; anti-HIV; nootropic;
KW   neuroprotective; antimicrobial; antiparkinsonian; cancer;
KW   immune system disorder; angiogenesis; hyperproliferative disorder;
KW   cardiovascular disorder; apoptosis; neurological disease;
KW   infectious disease; wound healing.
XX
OS   Homo sapiens.
XX
PN   WO200035937-A1.
XX
PD   22-JUN-2000.
XX
PF   16-DEC-1999;   99WO-US029950.
XX
PR   17-DEC-1998;   98US-0112809P.
PR   18-DEC-1998;   98US-0113006P.
XX
PA   (HUMA-) HUMAN GENOME SCI INC.
XX
PI   Ruben SM,  Ebner R,  Rosen CA,  Endress GA,  Soppet DR,  Ni J;
PI   Duan DR,  Moore PA,  Shi Y,  Lafleur DW,  Olsen HS,  Florence K;
XX
DR   WPI; 2000-431566/37.
DR   N-PSDB; AAA78407.
XX
PT   Forty seven human nucleic acids encoding secreted proteins, useful in the
PT   treatment, prevention and diagnosis of cancers, disorders of the immune
```

PT system, angiogenesis disorders, neurological diseases and
PT hyperproliferative disorders.
XX
PS Claim 11; Page 499; 562pp; English.
XX
CC The polynucleotide sequence given in AAA78381 to AAA78432 encode the
CC human secreted proteins given in AAB24437 to AAB24604. Human secreted
CC proteins have activities based on the tissues and cells the genes are
CC expressed in. Examples of activities include: cytostatic; antianaemic;
CC antidiabetic; antiinflammatory; ophthalmological; antirheumatic;
CC antiarthritic; antipsoriatic; antiangiogenic; cardiant; anti-HIV;
CC nootropic; neuroprotective; antimicrobial and antiparkinsonian. Human
CC secreted protein polynucleotides, polypeptides, antagonists and/or
CC agonists may be useful in treating, preventing, and/or diagnosing other
CC diseases, disorders, and/or conditions such as: (a) cancers; (b)
CC disorders of the immune system; (c) angiogenesis disorders; (d)
CC hyperproliferative disorders; (e) cardiovascular disorders; (f) diseases
CC associated with increase apoptosis; (g) neurological diseases; and (h)
CC infectious diseases. They are also used to promote wound healing.
CC AAA78372 to AAA78380 and AAB24436 represent sequences used in the
CC exemplification of the present invention
XX
SQ Sequence 258 AA;

Query Match 99.1%; Score 1355; DB 3; Length 258;
Best Local Similarity 99.2%; Pred. No. 7.9e-145;
Matches 255; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

```
Qy          1 MLLTLAGGALFFPGLFALCTWALRHSQPGWSRTDCVMISTRLVSSVHAVLATGSGIVIIR 60
              ||||||||||||||||||||||| ||||||||||||||||||||||||||||||||||||
Db          1 MLLTLAGGALFFPGLFALCTWALRRSQPGWSRTDCVMISTRLVSSVHAVLATGSGIVIIR 60

Qy         61 SCDDVITGRHWLAREYVWFLIPYMIYDSYAMYLCEWCRTRDQNRAPSLTLRNFLSRNRLM 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 SCDDVITGRHWLAREYVWFLIPYMIYDSYAMYLCEWCRTRDQNRAPSLTLRNFLSRNRLM 120

Qy        121 ITHHAVILLVLVPVAQRLRGDLGDFFVGCIFTAELSTPFVSLGRVLIQLKQQHTLLYKVN 180
              |||||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 ITHHAVILFVLVPVAQRLRGDLGDFFVGCIFTAELSTPFVSLGRVLIQLKQQHTLLYKVN 180

Qy        181 GILTLATFLSCRILLFPFMYWSYGRQQGLSLLQVPFSIPFYCNVANAFLVAPQIYWFCLL 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 GILTLATFLSCRILLFPFMYWSYGRQQGLSLLQVPFSIPFYCNVANAFLVAPQIYWFCLL 240

Qy        241 CRKAVRLFDTPQAKKDG 257
              |||||||||||||||||
Db        241 CRKAVRLFDTPQAKKDG 257
```

Notice to Comply	Application No. 10/536,772	Applicant(s) Gu et al.	
	Examiner Peter J. Reddig	Art Unit 1642	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The disclosure is lacking numerous sequence identifiers and sequence ID numbers, see the section titled "Sequence Listing" in the accompanying First Office Action on the Merits.

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☐ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application.**

☐ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
WASHINGTON, DC 20231
www.uspto.gov

APPLICATION NO. /CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
10/536,772	05/26/2005	Jianren Gu	186691/US

EXAMINER	
Peter Reddig, Ph.D.	
ART UNIT	**PAPER**
1642	

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant must provide the appropriate SEQ ID NO: for all sequences encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2).

If a complete reply has not been submitted by the time period set in the accompanying Office action has expired, this application will become abandoned under 37 CFR 1.821(g).

Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio (http://ww.uspto.gov/ebc/efs/downloads/documents.htm>, EFS Submission User Manual-ePAVE)

2. Mailed to

Mail Stop Sequence

Commissioner for Patents

P.O. Box 22313-1450

Alexandria, VA 22313-1450

3.Hand Carry, Federal Express, United Parcel Service or other delivery service to:

U. S. Patent and Trademark Office

Mail Stop Sequence

Customer Window

Randolph Building

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Reddig whose telephone number is 571-272-9031. The examiner can normally be reached on M-F 8:30 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foleycan be reached on 571-272-0890.

Peter Reddig, Ph.D.
Art Unit 1642

SUSAN UNGAR, PH.D
PRIMARY EXAMINER